

Remarks

The December 12, 2011 Official Action has been carefully reviewed. In view of the following remarks, favorable reconsideration and allowance of this application are respectfully requested.

The present remarks and amendments are being filed as part of the submission required under 37 C.F.R. §1.114, in connection with the Request for Continued Examination, which is submitted concurrently herewith.

At the outset it is noted that a shortened statutory response period of three (3) months was set forth in the December 12, 2011 Official Action. Therefore, the initial due date for response was March 12, 2012. Accordingly, a petition for a 1 month extension is presented with this response, which is being filed within the one month extension period.

Claims 1, 9, 13, 17, 20, 25, 29, and 34-37 have been rejected under 35 U.S.C. §102(b) as allegedly anticipated by U.S. Patent 6,323,219 (Costanzo).

Claims 1-4, 9, 13, 17-20, 25, 29, and 34-41 have been rejected under 35 U.S.C §103(a) for allegedly unpatentable over the '219 patent.

The foregoing rejections constitute all of the grounds set forth in the December 12, 2011 Official Action for refusing the present application.

In accordance with the instant amendment, Applicants have amended claims 1 and 17 and added new claims 42 and 43. Support for the amendments to claims 1 and 17 can be found throughout the application including, for example, at page 6, in Example IV, and in the claims as originally filed. Support for new claims 42 and 43 can be found throughout the application including, for example, at pages 1 and 5. No new matter has been introduced into this application by reason of any of the amendments presented herewith.

In view of the present amendment and the reasons set forth in this response, Applicants respectfully submit that the 35 U.S.C. §102(b) rejection 1, 9, 13, 17, 20, 25, 29, and

34-37 and the 35 U.S.C. §103(a) rejection of claims 1-4, 9, 13, 17-20, 25, 29, and 34-41, as set forth in the December 12, 2011 Official Action, cannot be maintained. These grounds of rejection are, therefore, respectfully traversed.

STATEMENT OF SUBSTANCE OF INTERVIEW

This Statement of Substance of Interview is being submitted in accordance with §713.04 of the Manual of Patent Examining Procedure to make of record a telephone interview held between Examiner Benjamin Packard, Miri Seiberg, and the undersigned on or about February 23, 2012. The Interview Summary Form dated March 8, 2012 indicated that a written reply to the last Official Action must include the Statement of Substance of Interview.

A telephonic interview was held on or about February 23, 2012 between the undersigned and Examiner Packard for the purpose of discussing the prior art rejections of claims 1-4, 9, 13, 17-20, 25, 29, and 34-41. At the outset, the undersigned indicated that in contrast to the Examiner's assertion at page 3 of the instant Official Action, the instant claims, in fact, recite topical application of the composition prior to exposure to ultraviolet radiation. Potential claim amendments were also discussed. No definitive agreement with respect to the claims was reached.

This Statement of Substance of Interview is being filed with the reply to the last Official Action in accordance §713.04 of the MPEP.

CLAIMS 1, 9, 13, 17, 20, 25, 29 AND 34-37 ARE NOT ANTICIPATED BY THE '219 PATENT

Claims 1, 9, 13, 17, 20, 25, 29, and 34-37 have been rejected under 35 U.S.C. §102(b) as allegedly anticipated by U.S. Patent 6,323,219. The '219 patent allegedly discloses a preparation of STI by grinding soybean in purified water and the application of the STI composition to the skin of swine.

It is the Examiner's position that any application of the above STI composition to skin would read on the instant methods. Applicants continue to respectfully disagree with the Examiner's position for the reasons of record and those set forth below.

At the outset, the Examiner states at page 3 of the instant Official Action that "the instant claims do not require application prior to exposure of skin to ultraviolet radiation." Applicants respectfully disagree. Indeed, lines 6-7 of claims 1 and claim 17 clearly, positively recite that the composition is applied to the skin prior to exposure to photocarcinogenic ultraviolet B radiation. Accordingly, the instant claims recite the topical application of the composition followed by exposure to ultraviolet B irradiation.

The Examiner cites Examples 12 and 13 of the '219 patent at page 3 of the instant Official Action in support of the instant rejection. In Example 12, soymilk was topically administered to dark-skinned Yucatan swine and depigmentation was observed. However, these laboratory animals were not exposed to ultraviolet B radiation, as required by the instant claims. Further, the instant claims have been amended to recite that the skin being treated is human skin. With regard to Example 13 of the '219 patent, the STI is applied to age spots. Age spots are skin damage caused by over-exposure to the sun's ultraviolet rays (see, e.g., www.agespots.net/causes.aspx). Inasmuch as the instant claims specifically recite the application of the composition to skin undamaged by ultraviolet radiation, it is clear that the methods of Example 13 of the '219 patent are not encompassed by the instant claims.

In view of the foregoing, it is clear that Examples 12 and 13 of the '219 patent do not teach each and every element of the instant claims.

At page 3 and 4 of the instant Official Action, the Examiner contends that the "patient population disclosed by the prior art reference here is entirely within the claimed

genus" and concludes that "the same steps were applied to the same patient population suggests the method was an inherent function." Applicants respectfully disagree with the Examiner's position.

The '219 patent (which was co-invented by Miri Seiberg, one of the co-inventors of the instant application) is concerned with "compounds which affect melanogenesis and can be used as depigmenting agents" (see Abstract). Specifically, the '219 patent demonstrates the application of their STI composition *after* ultraviolet application to skin. Indeed, as shown in Figure 4B, the '219 patent demonstrates that exposure of skin cells to UVB irradiation increased melanogenesis and pigmentation. Subsequent application of a trypsin inhibitor resulted in the depigmentation of the skin *already* exposed to and damaged by UVB irradiation. Accordingly, the patient populations are clearly different. In the '219 patent, the patients have already received skin damaging UV radiation resulting in the pigmented age spots. In stark contrast, the instant claims require the treatment of skin that is undamaged by ultraviolet radiation and requires topical application to the skin prior to exposure to UVB radiation.

In view of all of the foregoing, Applicants respectfully submit that the instant rejection under 35 U.S.C. §102(b) is untenable. Withdrawal of the rejection is respectfully requested.

**CLAIMS 1-4, 9, 13, 17-20, 25, 29 AND 34-41 ARE NOT RENDERED
OBVIOUS BY THE '219 PATENT**

Claims 1-4, 9, 13, 17-20, 25, 29, and 34-41 have been rejected under 35 U.S.C §103(a) for allegedly unpatentable over the '219 patent. It is the Examiner's position that even though the '219 patent does not specifically disclose administering STI compositions to cells which have not been damaged by UV radiation, it allegedly would have been obvious to do so as unwanted skin pigmentation

may occur in skin that has not been exposed to UV radiation. Applicants respectfully disagree with the Examiner's position for the reasons of record and those set forth below.

As stated hereinabove, the instant claims recite topical application of a composition comprising a non-denatured, Kunitz-type soybean trypsin inhibitor "**prior** to exposure of the human skin to photocarcinogenic ultraviolet B radiation." In contrast, the '219 patent teaches applying STI compositions to already pigmented skin (e.g., **after** skin has been exposed to UV radiation). The '219 patent broadly states that their methods (inclusive of treating inflammatory diseases and increasing pigmentation through the administration of other compounds) are "directed at preventing as well as treating disorders" (column 30). However, the '219 patent does not specifically teach the application of an STI composition **prior** to exposure to photocarcinogenic UVB radiation. Accordingly, in order to establish a *prima facie* case of obviousness, motivation and a reasonable expectation of success must be provided as to why the skilled artisan would alter the methods of the '219 patent. In view of the reasons of record and those set forth below, Applicants respectfully submit that the Examiner has failed to establish such a *prima facie* case of obviousness.

The '219 patent clearly teaches that soybean trypsin inhibitor (STI) is effective in inhibiting melanogenesis, the process by which melanin is made. As of the instant invention, the skilled artisan understood melanin provided protection for skin from harmful ultraviolet radiation. For example, Gilchrest et al. (N. Eng. J. Med. (1999) 340:1341-1348; previously submitted) teach that "poorly melanized skin is far more vulnerable than melanized skin to acute and chronic injury caused by ultraviolet radiation (sunburn and photoaging or *photocarcinogenesis*...)" (page 1343, left column; emphasis added). Gilchrest et al. further state that melanin "has a photoprotective function in the skin, directly absorbing ultraviolet photons as well as reactive oxygen

species generated by the interaction of ultraviolet photons with membrane lipids and cellular chromophores" (page 1343, left column). Notably, melanin levels are increased in response to ultraviolet injury of skin which results in "a long-lasting endogenous "sunscreen" with a measured sun protection factor of approximately 3 to 5" (page 1343, left column). Moreover, other studies have shown that the increased levels of melanin in dark skin reduces the amount of ultraviolet radiation that reaches the upper dermis 5 fold and reduces the risk of skin cancer 500-1000 fold when compared to Caucasian skin (see, e.g., the abstracts of Kaidbey et al. (J. Am. Acad. Dermatol. (1979) 1:249-260) and Kollias et al. (J. Photochem. Photobiol. B. (1991) 9:135-160); previously presented).

In view of the foregoing, it is evident that the skilled artisan understood that increased melanin levels protected skin from ultraviolet radiation and reduced cutaneous tumor and skin cancer development. However, the '219 patent teach that STI administration *decreases* the levels of pigmentation and melanin, thereby **directly** teaching away from the instantly claimed invention. Accordingly, as of the instant invention, the skilled artisan clearly would not have had the motivation or the expectation of success in topically applying non-denatured, soy products comprising non-denatured, Kunitz-type soybean trypsin inhibitor to *decrease* the risk of cutaneous tumor development in skin cells, as instantly claimed. Indeed, based on the above references, a skilled artisan clearly would have **avoided** applying depigmenting agents - such as STI as taught by the '219 patent - prior to exposure of UVB irradiation.

In addition to the above, Applicants note that new claims 42 and 43 recite that the skin is Caucasian skin. As stated hereinabove, it was known in the prior art that increasing melanin in Caucasian skin **reduces** the risk of UV-induced skin cancer by "500-1000 fold." Accordingly, it is self-evident that the skilled artisan would have no motivation

or an expectation of success in topically applying a composition taught in the prior art to inhibit melanogenesis prior to exposure to UVB for reducing the risk cutaneous tumor development.

In stark contrast to the above, the instant application provides unexpectedly superior results through the application of a composition comprising non-denatured, Kunitz-type soybean trypsin inhibitor. Indeed, Example 4 of the instant application demonstrates that the application of such a composition reduced or eliminated the formation of thymidine dimers, a hallmark of UV-induced DNA damage known to be involved in the formation of skin cancer. Moreover, Figures 1, 2, and 4 and Table 1 of parent application U.S. Patent Application No. 10/108,248 show that the Kunitz-type soybean trypsin inhibitor is an effective inhibitor of UV-induced tumor formation.

Inasmuch as the instant claims require application of the composition prior to photocarcinogenic UVB exposure and the reference cited by the Examiner directly teaches away from the instantly claimed invention in view of the understanding in the art at the time of the instant invention, Applicants respectfully submit that the instant obviousness rejection cannot be reasonably maintained. Withdrawal of the rejection is respectfully requested.

CONCLUSION

In view of the foregoing remarks, it is respectfully urged that the rejections set forth in the December 12, 2011 Official Action be withdrawn and that this application be passed to issue.

In the event the Examiner is not persuaded as to the allowability of any claim, and it appears that any outstanding issues may be resolved through a telephone interview, the Examiner is requested to telephone the undersigned attorney at the phone number given below.

If a fee is required or an overpayment is made, the Commissioner is authorized to charge or credit the deposit account of the undersigned, Account No. 04-1406.

Respectfully submitted,
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/Robert C. Netter, Jr./

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